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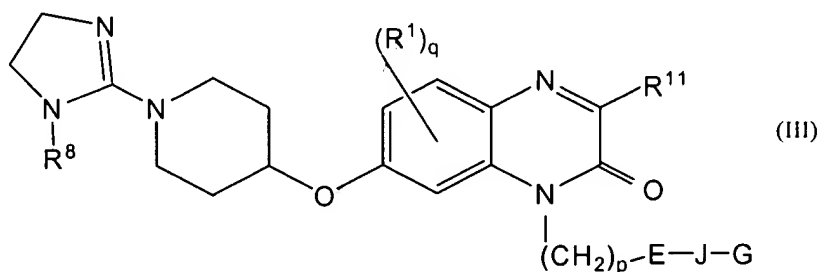
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Amendments to the Claims:

Please amend claims 5 and 10 to read as follows. All claims pending, including those unchanged by the present amendment, are reproduced below for the convenience of the Examiner. This listing of claims will replace all prior versions, and listings, of claims in the application:

1.-4. (Canceled)

5. (Currently amended) A compound of formula III:



wherein:

R^8 is selected from the group consisting of H, -OH, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, a five to ten membered heterocyclic ring system having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6} alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S;

R^1 is a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, halogen, polyhaloalkyl, C_{0-8} alkyl-C(=O)OH, C_{0-8} alkyl-C(=O)O- C_{1-8} alkyl, -CN, -NO₂, C_{1-8} alkyl-OH, C_{0-8} alkyl-SH, -C(=O)NR²R³, -O-R² and -O-C(=O)R², an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, polyhaloalkyl, -SO₂R², C_{0-8} alkyl-C(=O)OH and C_{0-8} alkyl-C(=O)O- C_{1-8} alkyl, ~~where R^2 and R^3 is as described above;~~

C' R^2 and R^3 are independently is selected from the group consisting of H, -OH, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, a five to ten membered heterocyclic ring system having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6} alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S;

q is 0-3;

R^{11} is a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, C_{1-6} alkylaryl, C_{1-6} alkyl- C_{3-8} cycloalkyl, $-O-R^2$, $-O-C(=O)R^2$, $-C_{1-8}$ alkyl- $O-R^{10}$, $-C_{1-8}$ alkyl- $O-C(=O)R^{10}$, $-C_{1-8}$ alkyl- $C(=O)OR^{10}$, $-C_{1-8}$ alkyl- $O-C(=O)OR^{10}$, $-C_{1-8}$ alkyl- $C(=O)NR^{10}R^{10}$, $-C_{1-8}$ alkyl- $NR^{10}R^{10}$, $-C_{1-8}$ alkyl- $NR^{10}C(=O)R^{10}$, $-SR^{10}$, where R^2 is as described above and R^{10} is a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, and wherein when two R^{10} groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

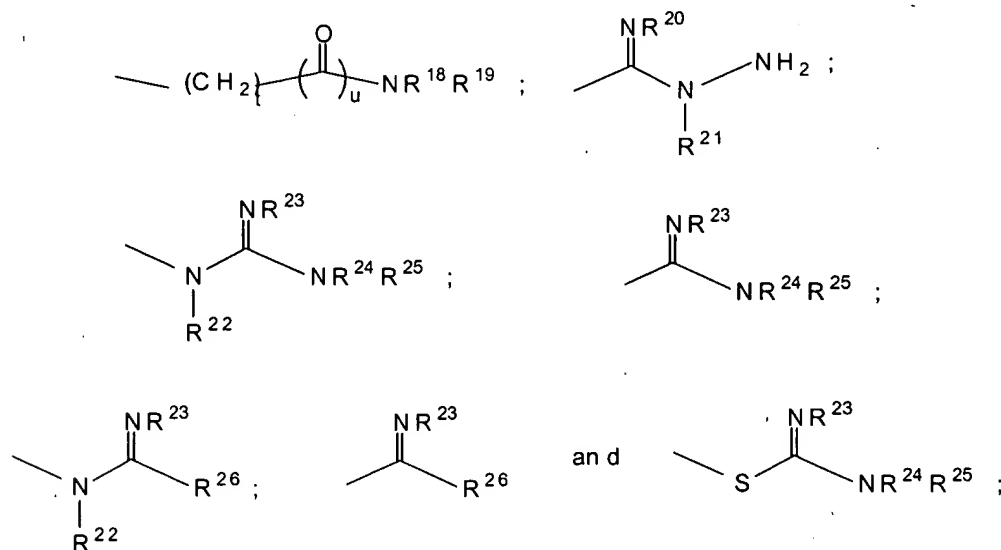
p is an integer from 0-2;

E is a member selected from the group consisting of a direct link, $-O-$, $-N(-R^{11})-$, where R^{11} is as set forth above, phenylene, a bivalent 5 to 12 member heteroaryl group having 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system having 1-4 heteroatoms selected from the group consisting of N, O and S, wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R^{14} groups;

J is a member selected from the group consisting of a direct link, a bivalent C_{3-8} cycloalkyl group, phenylene, a 5 to 12 member bivalent heteroaryl group having 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system having 1-4 heteroatoms selected from the group consisting of N, O and S wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R^{14} groups;

each R^{14} group is a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, halogen, polyhaloalkyl, C_{0-8} alkyl-C(=O)OH, C_{0-8} alkyl-C(=O)O- C_{1-8} alkyl, -CN, -NO₂, C_{1-8} alkyl-OH, C_{0-8} alkyl-SH, -O- R^2 and -O-C(=O) R^2 , an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, polyhaloalkyl, C_{0-8} alkyl-C(=O)OH and C_{0-8} alkyl-C(=O)O- C_{1-8} alkyl;

G is a member selected from the group consisting of: H; -CN; -OR¹⁷;



wherein

t is an integer from 0 to 6,

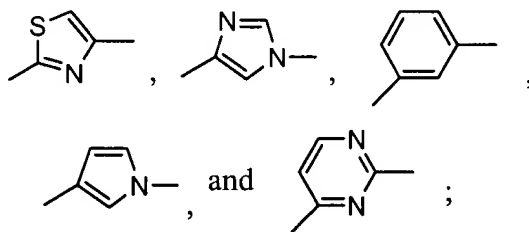
u is the integer 0 or 1, and R^{17} , R^{18} , R^{19} , R^{20} , R^{21} , R^{22} , R^{23} , R^{24} , R^{25} and R^{26} are independently selected from the group consisting of H, -OH, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, a five to ten membered heterocyclic ring system having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6} alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where R^{18} taken with R^{19} , R^{22} taken with either of R^{24} and R^{25} ,

60 and R²⁴ taken with R²⁵, can each independently form a 5 to 6 membered heterocyclic ring having
61 from 1 to 4 atoms selected from the group consisting of N, O and S;
62 with the proviso that when G is H, -CN, -OR¹⁷, either E or J must contain at least one N
63 atom;
64 or a pharmaceutically acceptable diastereomer, salt, hydrate, and solvate thereof.

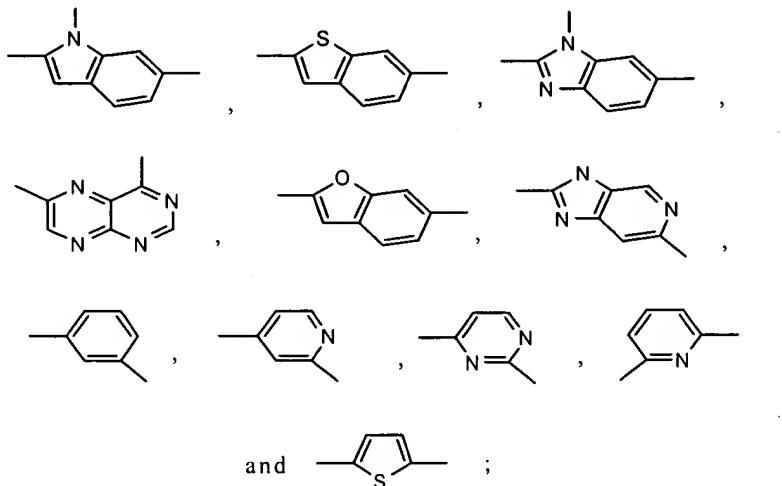
1 6. (Original) A compound of claim 5, wherein R¹ and R⁸ are independently a
2 lower alkyl group and R¹¹ is hydrogen or is a C₁ to C₈ alkyl group.

1 7. (Original) A compound of claim 5, wherein q is zero and R⁸ is lower alkyl
2 group.

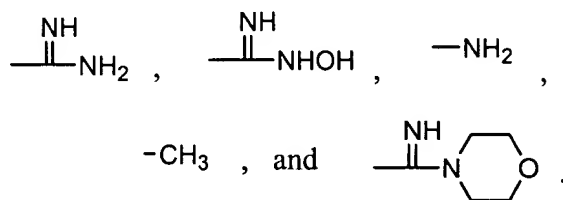
1 8. (Original) A compound of claim 5, wherein:
2 R⁸ is a methyl group;
3 p is an integer from 1-2;
4 E is selected from the group consisting of: a direct link,



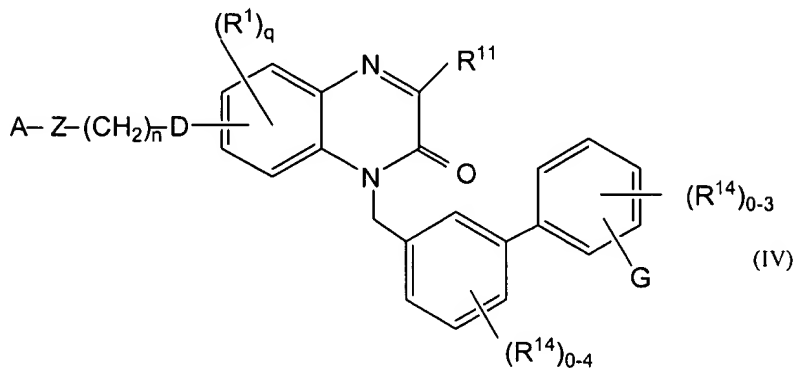
6 J is selected from the group consisting of:



8 and G is selected from the group consisting of:

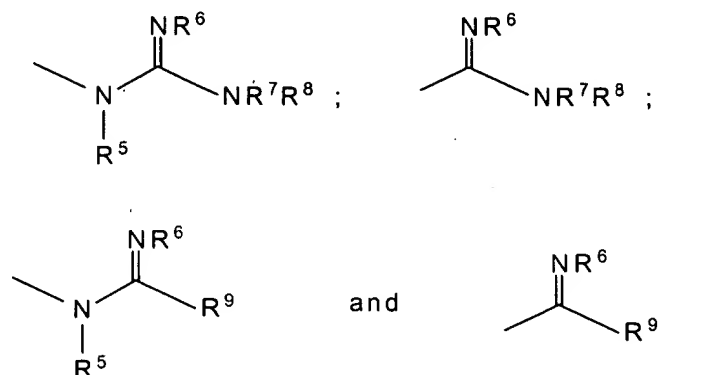


9. (Previously amended) A compound of formula IV:



wherein:

A is a member selected from the group consisting of: R², -NR³R⁴, -C(=O)NR³R⁴,



where R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , and R^9 are independently selected from the group consisting of H, -OH, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, a five to ten membered heterocyclic ring system having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6} alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where R^6 taken with either of R^7 and R^8 , and/or R^7 taken with R^8 , can each form a 5 to 6 membered heterocyclic ring having from 1 to 4 atoms selected from the group consisting of N, O and S;

Z is a member selected from the group consisting of a direct link, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} carbocyclic aryl, or a five to ten membered heterocyclic ring system having 1-4 heteroatoms selected from the group consisting of N, O and S;

n is 0-3;

D is a member selected from the group consisting of: $-CH_2-$, $-O-$, $-N R^2$, $-C(=O)-$, $-S-$, $-SO_2-$, $-SO_2-NR^2$, $-NR^2-SO_2$, $-OC(=O)-$, $-C(=O)NR^2$, and $-NR^2-C(=O)-$;

R^1 and R^{14} are independently a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, halogen, polyhaloalkyl, C_{0-8} alkyl- $C(=O)OH$, C_{0-8} alkyl- $C(=O)O-C_{1-8}$ alkyl, $-CN$, $-NO_2$, C_{1-8} alkyl-OH, C_{0-8} alkyl-SH, $-O-R^2$ and $-O-C(=O)R^2$, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, polyhaloalkyl,

26 C_{0-8} alkyl-C(=O)OH and C_{0-8} alkyl-C(=O)O- C_{1-8} alkyl;

27 q is 0-3;

28 R^{11} is a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl,

29 C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, C_{1-6} alkylaryl, C_{1-6} alkyl- C_{3-8} cycloalkyl, -O- R^2 ,

30 -O-C(=O) R^2 , - C_{1-8} alkyl-O- R^{10} , - C_{1-8} alkyl-O-C(=O) R^{10} , - C_{1-8} alkyl-C(=O)OR¹⁰,

31 - C_{1-8} alkyl-O-C(=O)OR¹⁰, - C_{1-8} alkyl-C(=O)NR¹⁰R¹⁰, - C_{1-8} alkyl-NR¹⁰R¹⁰,

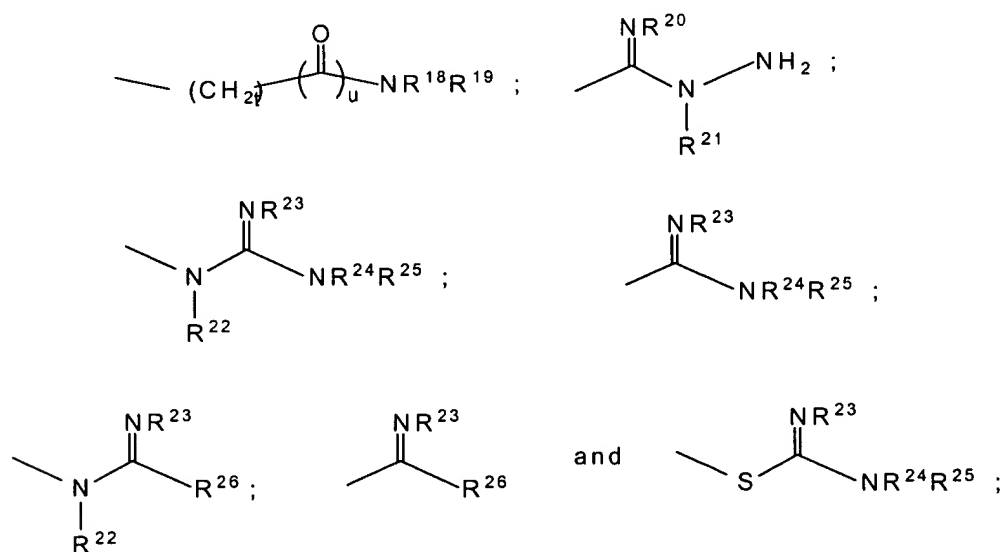
32 - C_{1-8} alkyl-NR¹⁰C(=O) R^{10} , -SR¹⁰, where R^2 is as described above and R^{10} is a member selected

33 from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, and wherein when two R^{10}

34 groups are present they may be taken together to form a saturated or unsaturated ring with the

35 atom to which they are both attached;

36 G is a member selected from the group consisting of: H; -CN; -OR¹⁷;



38 wherein

39 t is an integer from 0 to 6,

40 u is the integer 0 or 1, and R^{17} , R^{18} , R^{19} , R^{20} , R^{21} , R^{22} , R^{23} , R^{24} , R^{25} and R^{26} are

41 independently selected from the group consisting of H, -OH, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl,

42 C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, a five to ten membered heterocyclic ring system having 1-4

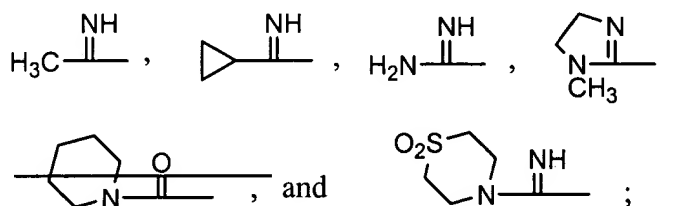
heteroatoms selected from the group consisting of N, O and S; and C₁₋₆alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where R¹⁸ taken with R¹⁹, R²² taken with either of R²⁴ and R²⁵, and R²⁴ taken with R²⁵, can each independently form a 5 to 6 membered heterocyclic ring having from 1 to 4 atoms selected from the group consisting of N, O and S;

with the proviso that when G is H, -CN, -OR¹⁷, either E or J must contain at least one N atom;

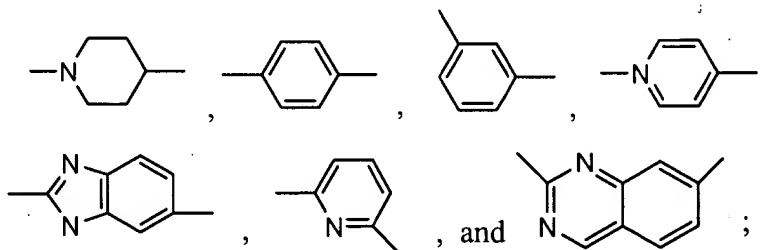
or a pharmaceutically acceptable diastereomer, salt, hydrate, and solvate thereof.

10. (Currently amended) A compound of claim 9, wherein R¹, R⁸, R¹¹ and R¹⁴ are independently selected from the group consisting of hydrogen, methyl and ethyl;

A is selected from the group consisting of: -H, -CH₃, -NH₂, -C(O)N(CH₃)₂,



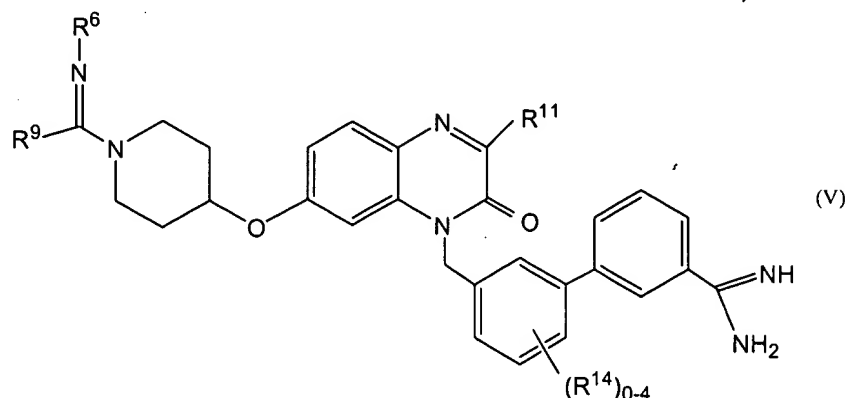
Z is selected from the group consisting of:



n is an integer from 0-2; and

D is selected from the group consisting of: -O-, -N(CH₃)-, and -CH₂-.

11. (Previously amended) A compound of formula V:



wherein:

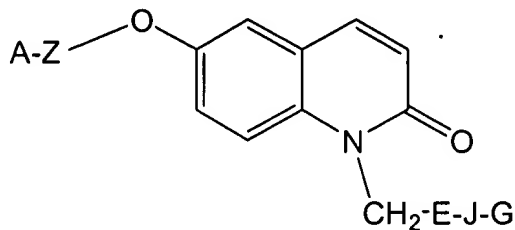
R^2 , R^6 , and R^9 are independently selected from the group consisting of H, -OH, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, a five to ten membered heterocyclic ring system having 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6} alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S;

R^{11} is independently a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, C_{1-6} alkylaryl, C_{1-6} alkyl- C_{3-8} cycloalkyl, -O- R^2 , -O-C(=O) R^2 , - C_{1-8} alkyl-O- R^{10} , - C_{1-8} alkyl-O-C(=O) R^{10} , - C_{1-8} alkyl-C(=O)OR¹⁰, - C_{1-8} alkyl-O-C(=O)OR¹⁰, - C_{1-8} alkyl-C(=O)NR¹⁰R¹⁰, - C_{1-8} alkyl-NR¹⁰R¹⁰, - C_{1-8} alkyl-NR¹⁰C(=O)R¹⁰, -SR¹⁰, where R^2 is as described above and R^{10} is a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, and wherein when two R^{10} groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

each R^{14} group is a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, halogen, polyhaloalkyl, C_{0-8} alkyl-C(=O)OH, C_{0-8} alkyl-C(=O)O- C_{1-8} alkyl, -CN, -NO₂, C_{1-8} alkyl-OH, C_{0-8} alkyl-SH, -O- R^2 and -O-C(=O) R^2 , an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, polyhaloalkyl,

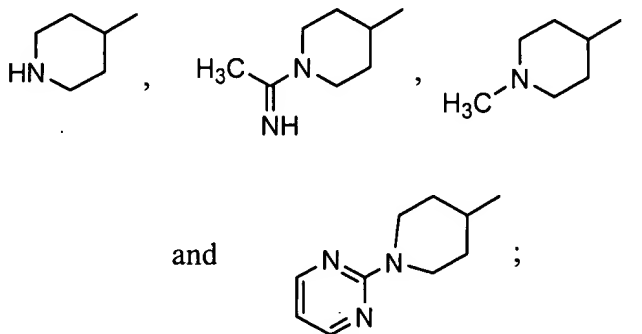
- 23 C₀₋₈alkyl-C(=O)OH and C₀₋₈alkyl-C(=O)O-C₁₋₈alkyl;
24 or a pharmaceutically acceptable diastereomer, salt, hydrate, and solvate thereof.

12. (Original) A compound having the following structure:



wherein:

A-Z is a member selected from the group consisting of:



C'



8

1

1

1

5 a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke,
6 transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus,
7 coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura,
8 thromboangiitis obliterans, thrombotic disease associated with heparin-induced
9 thrombocytopenia, thrombotic complications associated with extracorporeal circulation,
10 thrombotic complications associated with instrumentation such as cardiac or other intravascular
11 catheterization, intra-aortic balloon pump, coronary stent or cardiac valve, and conditions
12 requiring the fitting of prosthetic devices.

1 16. (Previously amended) A method for inhibiting the coagulation of
2 biological samples comprising the administration of a compound as in one of claims 5-12.
